

Pattern formation in a cell based auxin transport model with numerical bifurcation analysis

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Abstract

Transport models of growth hormones can be used to reproduce the hormone accumulations that occur in plant organs. Mostly, these accumulation patterns are calculated using time step methods, even though only the resulting steady state patterns of the model are of interest. We examine the steady state solutions of the hormone transport model of Smith et al (2006) for a one-dimensional row of plant cells. We search for the steady state solutions as a function of three of the model parameters by using numerical continuation methods and bifurcation analysis. These methods are more adequate for solving steady state problems than time step methods. We discuss a trivial solution where the concentrations of hormones are equal in all cells and examine its stability region. We identify two generic bifurcation scenarios through which the trivial solution loses its stability. The trivial solution becomes either a steady state pattern with regular spaced peaks or a pattern where the concentration is periodic in time.

keywords: Bifurcation analysis pattern formation parameter dependence auxin transport model stability periodic solution pattern

1 Introduction

1.1 Biological background

For centuries, the formation of well-defined patterns in plants, such as the orientation and shape of leaves, their venation patterns, the spatial distribution of hairs and stomata, the early embryonic development patterns and the branching patterns in both root systems and treetops, has intrigued many scientists. Experimental research has identified a number of molecular components that play a major role in several of these pattern formation processes. One of them is the plant hormone auxin, and more specifically the auxin molecule Indol-3-Acetic Acid (IAA). Experiments have shown that the active directional transport, which leads to accumulation spots of the auxin hormone, plays a central part in the pattern formation (Scarpella et al, 2006; Benková et al, 2003; Bilborough et al, 2011).

Based on such experimental evidence, Reinhardt *et al.* developed a conceptual model that describes the auxin transport through the cells (Reinhardt et al, 2003). Smith and collaborators then constructed a computational simulation model (Smith et al, 2006) incorporating the experimental evidence that the transport of the auxin molecule IAA is driven by a pumping mechanism that is mediated by PIN1 proteins located at the cell membrane in addition to diffusion (Palme and Gälweiler, 1999). Therefore, Smith and collaborators modeled the transport of the IAA hormone through the cells by describing the simultaneous evolution of the PIN1 protein and the IAA hormone concentrations over time. Also other computational models were developed based on these molecular mechanisms identified by Reinhardt *et al.*. For instance Jönsson *et al.* proposed a phyllotaxis model based on the polarized auxin transport (Jönsson et al, 2006). They analyzed a simplified version of their model that assumes an equal and constant PIN1 concentration in every cell and membrane. In their simulations they used a linear row of uniform cells with periodic boundary conditions. The results show that the spacing and the number of peaks in this simplified model depends on the different parameters. Jönsson and collaborators also performed a stability analysis and found an analytical expression for the eigenvalues, belonging to a solution pattern with equal auxin concentrations. The eigenvalues are all real and a function of the model parameters of the model. They also identified the parameter threshold where the largest eigenvalue becomes unstable. Beyond this threshold, all solutions will contain auxin peaks.

This paper expands the study of the steady states in the transport of hormones. We limit ourselves to the study of the auxin distribution in a linear row of uniform cells that represents, for example, a cross section through a young leaf. We perform a thorough mathematical exploration of the behavior of the models and how their equations are solved starting from the coupled model of Smith et al (2006). In contrast to the analysis of Jönsson *et al.* on a row of

cells where the concentration of PIN1 was fixed, we will use a coupled model where the PIN1 concentration is allowed to change from cell to cell. The analysis gives new insights into the spacing of auxin accumulations that form the basis of vascular development (Scarpella et al, 2006).

The main contribution of the paper is a systematic numerical bifurcation analysis for the coupled model describing the transport of growth hormones. The analysis identifies two generic bifurcation scenarios that reappear for various choices of the parameters of the problem. Through the bifurcation diagrams we identify the genesis of the patterns that were observed by Smith and collaborators. Furthermore, we have found a limited parameter range that allows periodic solutions in the system. In these solutions, the concentration of auxin of each cell varies periodically over time. To the knowledge of the authors these results have not appeared in the literature.

We present our work as follows. In section 1.2 the basic cell polarization and auxin transport model of Smith *et al.*, where PIN1 is allowed to change, is reconstructed using graph theory to describe the geometry and connectivity of the cells. In the next section, a specific model that will be used in the simulations is defined. In Smith et al (2006) the model roughly correlates to a ring of cells around an axial plant organ. In subsequent situations we consider a linear row of cells running from the margin to the midvein of the leaf and we consider the fluxes at the boundary of the leaf. We will describe this by using Neumann boundary conditions instead of periodic boundary conditions which is explained in section 2.1. Also in this section we look at the different parameter values. Similar to Smith *et al.*, we use time integration to solve the coupled model of Smith *et al.* in section 2.2. Since we are only interested in the steady state solutions, we define in section 2.3, the corresponding steady state system. For this steady state model, we define in section 3 a trivial solution and its stability properties. The stability is dependent on the model parameters and we examine for which parameter regions the trivial solution is stable. Section 4 contains the techniques that will be used to solve the model. In particular, we will discuss bifurcation analysis (4.1) and continuation methods (4.2). Bifurcation analysis reveals the relation between the stability of a solution and the model parameters and continuation methods calculates approximate solutions in function of a model parameter. In section 5 we show the results of our simulations. In section 6 we conclude and give an outlook.

1.2 Description of the mathematical model

Before constructing a compartmental model that describes the concentration of growth hormones per cell and its transport through a plant organ such as for example a leaf, its geometry must be specified. We do this with the help of graph theory.

1.2.1 Geometry of the cells

The two-dimensional model of a leaf consists of cells and cell walls and the geometry can be considered as a structure of piecewise linear cell walls. We represent this structure of cell walls by a graph $G(E, V)$ with edges E and vertices V . In this graph the set of edges E represents the cell walls of the leaf. Each edge connects a pair of vertices, the endpoints of a cell wall. We label the vertices with the letters k and l ($k, l \in V$) and an edge with the tuple (k, l) . Another characteristic of a cell wall is that it has no direction. The edge (k, l) represents the same edge as (l, k) and we refer to it with the pair $\{k, l\}$. Because cell walls only intersect at their endpoints, the graph G is a planar undirected graph. Each cell wall has a length and therefore the graph is also a weighted graph. We denote these weights, the length of the cell wall $\{k, l\}$, as l_{kl} . In the model of Smith et al (2006), only the length of the wall that separates two cells is important and not its shape. We therefore assume in this case that there exists at most one straight edge that separates two different faces of the graph G .

A graph G that represents the geometry of a leaf is displayed with full lines on figure 1. A cell in this model of the leaf is a face of the planar graph G . We refer to a cell with the letters i and j . As a consequence a cell is a vertex in the weak dual undirected graph $H(\tilde{E}, \tilde{V})$ of graph $G(E, V)$ (displayed on figure 1 with dashed lines). In this graph H every vertex $i \in \tilde{V}$ represents a cell and every edge $\{i, j\} \in \tilde{E}$ represents the connection between two neighboring cells and is therefore always undirected. Because an edge is the connection between neighboring cells, we can define the neighboring cells of a cell in the leaf. They are represented by the adjacent vertices of vertex i denoted as $\mathcal{N}_i \subset \tilde{V}$. Furthermore, the dual graph H is, just like graph G , a weighted graph with the same weights as G . Indeed, for each edge $\{i, j\} \in \tilde{E}$ we associate one edge $\{k, l\} \in E$ which represents their common cell wall. Thus we can associate the length of the cell wall l_{kl} with $\{i, j\}$. We denote it with l_{ij} .

The graphs G and H represent the geometry of a group of cells in a 2D plant organ at a certain moment in time. In advanced models this geometry changes over time because cell walls grow and cells divide (Smith et al, 2006), but in this paper we look at the basic, coupled cell polarization and auxin transport model of Smith *et al.* and the geometry is assumed to be static. As a consequence also the graphs G and H are fixed.

1.2.2 Transport of growth hormones

With the help of the geometry it is now possible to formulate a model for the transport of the growth hormones through the cells. We will formulate the coupled basic model of Smith et al (2006) applied to a section across a leaf with the geometry specified above.

In every cell i two substances play an important role in the growth process:

- The concentration of proteins PIN1 in cell i , which is time dependent, is

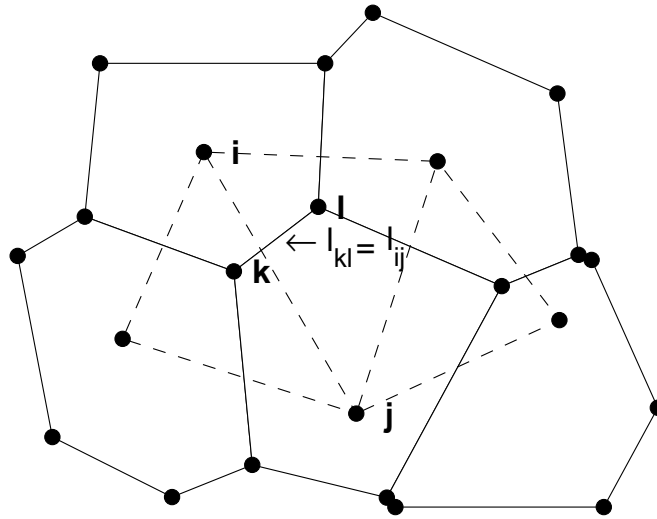


Figure 1: A graph (solid line) and its weak dual graph (dashed line) that models the static geometry of the cells. The edges of the graph are modeling the cell wall and only the length plays a role in the hormone transport. These lengths l_{kl} are the weights associated with the edge between vertex k and l . Similarly, each edge of the weak dual gets a weight corresponding to the length of the wall between cell i and j . So it gets the same weight $l_{ij} = l_{kl}$.

denoted as $p_i(t) \in \mathbb{R}^+$,

- The concentration of the hormone IAA in cell i , also known as auxin, is also time dependent and is denoted as $a_i(t) \in \mathbb{R}^+$.

The model describes the evolution of these concentrations in each cell. This evolution depends in a non-linear way on the concentrations of the neighboring cells. The value of $p_i(t)$ is determined by the production and decay of PIN1. Its time evolution for each cell $i \in \tilde{V}$ is modeled by

$$\frac{dp_i(t)}{dt} = \frac{\rho_{\text{PIN}_0} + \rho_{\text{PIN}} a_i(t)}{1 + \kappa_{\text{PIN}} p_i(t)} - \mu_{\text{PIN}} p_i(t), \quad (1)$$

where $\rho_{\text{PIN}_0} \in \mathbb{R}^+$ is the base production of PIN1 proteins, $\rho_{\text{PIN}} \in \mathbb{R}^+$ is a coefficient capturing the up-regulation of PIN1 production by auxin, $\kappa_{\text{PIN}} \in \mathbb{R}^+$ is the saturation coefficient of the PIN1 production and $\mu_{\text{PIN}} \in \mathbb{R}^+$ is the PIN1 decay constant. This means that the evolution of $p_i(t)$ in time depends strictly on the concentration in the cell itself.

The concentration of IAA in a cell depends on more factors than the production and the decay of auxin in the cell. Change of $a_i(t)$ is also determined by diffusion (passive transport) and active transport of auxin between the cells. The change over time of the concentration of IAA is modeled by the equation

$$\begin{aligned} \frac{da_i(t)}{dt} = & \frac{\rho_{\text{IAA}}}{1 + \kappa_{\text{IAA}} a_i(t)} - \mu_{\text{IAA}} a_i(t) - \sum_{j \in \mathcal{N}_i} D(a_i(t) - a_j(t)) \\ & + \sum_{j \in \mathcal{N}_i} (\text{ActiveTransport}_{j \rightarrow i} - \text{ActiveTransport}_{i \rightarrow j}), \end{aligned} \quad (2)$$

where $\rho_{\text{IAA}} \in \mathbb{R}^+$ is the IAA production coefficient, $\kappa_{\text{IAA}} \in \mathbb{R}^+$ is the coefficient which controls the saturation of IAA production, $\mu_{\text{IAA}} \in \mathbb{R}^+$ is the IAA decay constant and $D \in \mathbb{R}^+$ is the IAA diffusion coefficient. The active transport depends on the presence of PIN1 denoted by p_i and is modeled by the formula

$$\text{ActiveTransport}_{i \rightarrow j} = T \left(\frac{p_i(t) l_{ij} b^{a_j(t)}}{\sum_{k \in \mathcal{N}_i} l_{ik} b^{a_k(t)}} \right) \frac{a_i(t)^2}{1 + \kappa_T a_j(t)^2}, \quad (3)$$

where $T \in \mathbb{R}^+$ is a polar IAA transport coefficient, $b \in \mathbb{R}^+$ is the exponentiation base which controls the extent to which the PIN1 protein distribution is affected by the neighboring cells and $\kappa_T \in \mathbb{R}^+$ is an IAA transport saturation coefficient. From equation (2) we know that the evolution of $a_i(t)$ depends only on itself, the first and the second neighbors of cell i . With the constructed graphs these neighbors can be determined easily since these are all the vertices in graph H with a distance to vertex i that is at most two.

Equations (1), (2) and (3) describe the coupled model of Smith *et al.* that has been used to study the transport of hormones in the Arabidopsis shoot apex. In Smith et al (2006) they have studied a row of 50 equal sized cells with periodic boundary conditions. The time evolution starting from an initially flat

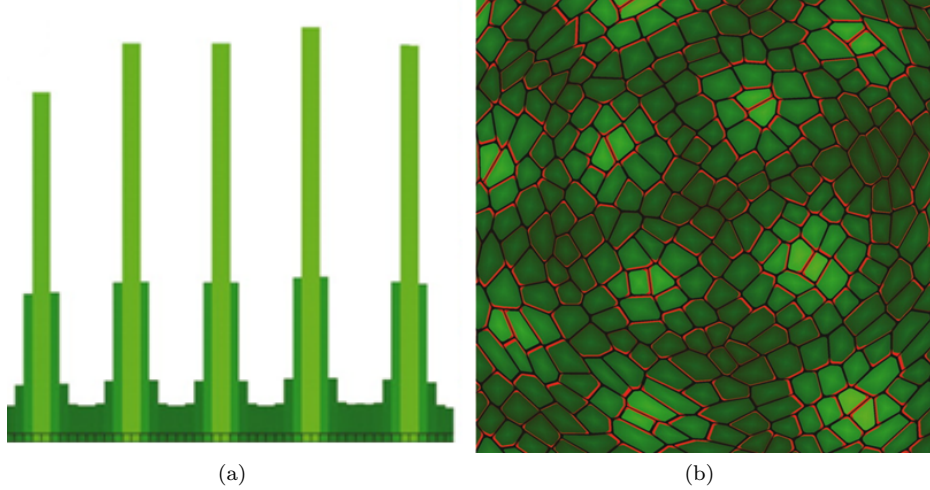


Figure 2: Simulation results of Smith *et al.* for a one dimensional row of 50 cells with periodic boundary conditions and a two dimensional grid of irregular cells. The shades of green show a difference in the IAA concentration. The red shows the PIN1 concentration (figure reproduced from Smith et al (2006)).

solution with a small amount of noise to break symmetry, showed the emergence of a pattern in the IAA concentrations (figure 2a). Some cells have a very high concentration of the growth hormone. This results in a pattern with peaks that are equally spaced and become more prominent for an increasing IAA transport coefficient T .

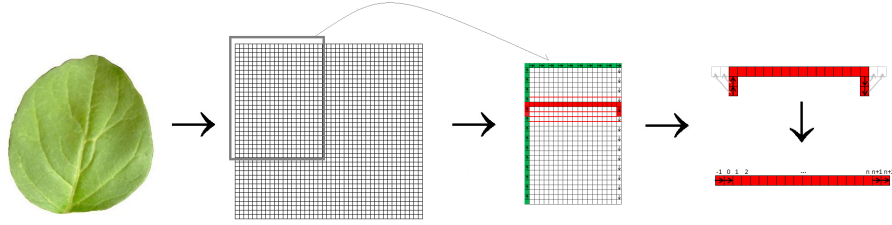
Similar patterns emerge in two dimensional models. There the cell shape is irregular. Again a pattern emerges with some cells having a high concentration of the growth hormone IAA (figure 2b).

2 The simulation problem

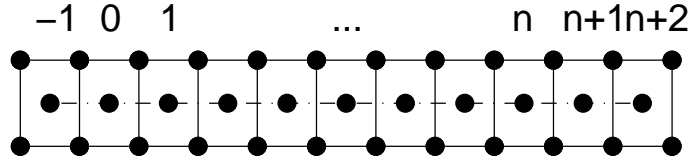
2.1 The domain, its boundary conditions and the parameters

In this paper we analyze the solutions of equations (1) and (2), the coupled model of Smith *et al.*, for a one dimensional file of equal sized square cells. This row of cells represents a part of the leaf from the left margin to the midvein. To provide the boundary conditions, two ghost cells are required at the end of the domain, since the model relates each cell with two cells at the left and the right (figure 3a).

The graph and its weak dual for the one-dimensional domain are shown in figure 3b. The length of each cell wall is equal to l . The set of vertices \hat{V} of the



(a)



(b)

Figure 3: (a) The one-dimensional model can be seen as a row of cells cut out of a leaf with equal sized square cells. In the first step we represent the leaf as a two dimensional squared grid of equal sized square cells. The second arrow indicates that we only consider the part from the left margin till the midvein. Here in each cell at the boundary, the direction of the auxin fluxes is indicated. In the third step a horizontal row of inner cells with, at each side two boundary cells is cut out of the domain. In the last step this domain is enrolled so it forms a one dimensional file of equal sized square cells. The two boundary cells at each side of the domain are the ghost cells. (b) The geometry of the leaf, used in the simulations, is a one-dimensional row of equal sized square cells. The weak dual is a row of connected cells. Each cell has a concentration of auxin that is denoted by $a_i(t)$ and a concentration of PIN1 that is denoted by $p_i(t)$. The cells 1 to n contain the unknowns, the cells -1 , 0 , $n+1$ and $n+2$ are ghost cells where the concentrations are set such that it produces in- and outgoing fluxes.

weak dual graph is split in n interior cells and four ghost cells, two on each side. The n interior points are labeled 1 to n . The ghost cells are cell -1 and 0 at the left of the domain and cell $n+1$ and $n+2$ at the right.

The concentration of the IAA hormone in the two ghost cells on each side are chosen to describe the influx at the boundary of the leaf and the efflux at the vein. The IAA concentration then changes linearly at the boundaries as if Neumann boundary conditions are applied. Until mentioned otherwise we will assume that the amount of influx is equal to the amount of efflux. This means that the boundary conditions become

$$\begin{cases} a_{-1}(t) = a_1(t) + 2\gamma & \text{and} & a_0(t) = a_1(t) + \gamma, \\ a_{n+1}(t) = a_n(t) - \gamma & \text{and} & a_{n+2}(t) = a_n(t) - 2\gamma. \end{cases} \quad (4)$$

The value of $p_0(t)$ and $p_{n+1}(t)$ in the ghost cells is determined by equation (1) that couples it to the value of $a_i(t)$ in the ghost cell. Note that $p_{-1}(t)$ and $p_{n+2}(t)$ do not appear in the problem since equation (3) does not require it. Together with an initial condition, the problem is transformed in an initial value problem that we can solve numerically with a time step method. Remark that these (homogeneous) Neumann boundary conditions are different from periodic boundary conditions. The concentrations in the cells on the left side of the domain can indeed be different from the concentrations in the cells on the right side of the domain.

Equations (1), (2) and (3) contain 11 parameters. A short description can be found in table 1 and further details can be found in Smith et al (2006). The values of these parameters must be real and positive. For the simulations in this paper we used three different parameter sets, M1, M2 and M3. Parameter set M2 corresponds with the values used by Smith et al (2006). Parameter set M1 and M3 contain the same values for the parameters as set M2 except for the IAA production coefficient. The value of this parameter is higher in parameter set M1 and lower in set M3.

2.2 Time integration

Similar to Smith *et al.*, we can solve the initial value problem with numerical integration. Analysis of the eigenvalues of the Jacobian shows that they are mostly located along the negative real axis with some small complex conjugate outliers at the left of the imaginary axis. This suggests that the fourth order Runge-Kutta method (Hairer et al, 2009) with time step $\Delta t = 0.01$ results in a stable method to integrate the equations. In figure 4 the time evolution is shown from $t = 0$ to $t = 10$. The domain contains 20 cells plus 4 ghost cells where we assume zero Neumann boundary conditions. The parameter values of set M1 are used and the initial value for the concentration is

$$p_i(t=0) = 5.4 \quad \text{and} \quad a_i(t=0) = 3.4, \quad (5)$$

where a small perturbation $0.2 \sin((5(i+2)\pi)/24)$ for $i = 1, \dots, 20$ was added to it to break symmetry.

Table 1: Values of the parameters of equations (1)–(3) used in the simulations. The parameter values of M2 are found in Smith et al (2006).

Symbol	Description	Value		
		M1	M2	M3
b	Base for exponential PIN allocation	3.000	3.000	3.000
κ_{PIN}	PIN saturation coefficient	1.000	1.000	1.000
κ_{T}	Transport saturation coefficient	1.000	1.000	1.000
κ_{IAA}	IAA saturation coefficient	1.000	1.000	1.000
ρ_{PIN_0}	Base production of PIN	0.000	0.000	0.000
ρ_{PIN}	PIN production coefficient	1.000	1.000	1.000
μ_{PIN}	PIN decay coefficient	0.100	0.100	0.100
μ_{IAA}	IAA decay coefficient	0.100	0.100	0.100
ρ_{IAA}	IAA production coefficient	1.500	0.750	0.500
D	IAA diffusion coefficient	1.000	1.000	1.000
T	IAA transport coefficient	3.500	3.500	3.500

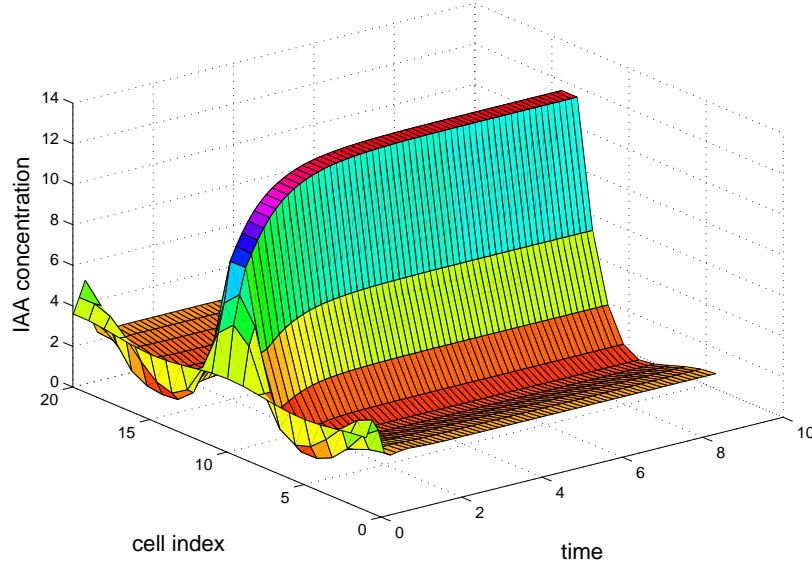


Figure 4: The time evolution of the solution for a row of 20 cells with zero Neumann boundary condition and parameter set M1. The initial condition is given by equation (5) and we used RK4 for numerical integration.

Figure 4 shows the development of a pattern in the concentration of the growth hormone IAA. After a certain time the pattern arrives in a stable steady state. For the row of 20 cells a single peak with a high IAA concentration is formed.

2.3 Steady state problem

Rather than evolving the system in time, we can calculate the steady state solutions directly. We rewrite equations (1), (2) and (3) in order to obtain the steady state equations for this specific geometry and boundary conditions. Because the length of each cell wall is constant, l , it cancels from the equation since it appears both in the numerator and denominator of equation (3). The steady state problem becomes:

$$\left\{ \begin{array}{l} 0 = \frac{\rho_{\text{PIN}_0} + \rho_{\text{PIN}} a_i}{1 + \kappa_{\text{PIN}} p_i} - \mu_{\text{PIN}} p_i \quad \text{with } i = 0, 1, \dots, n, n+1 \\ 0 = \frac{\rho_{\text{IAA}}}{1 + \kappa_{\text{IAA}} a_i} - \mu_{\text{IAA}} a_i - D(a_i - a_{i-1}) - D(a_i - a_{i+1}) \\ \quad + T \left(\frac{p_{i-1} b^{a_i}}{b^{a_{i-2}} + b^{a_i}} \right) \frac{a_{i-1}^2}{1 + \kappa_T a_i^2} - T \left(\frac{p_i b^{a_{i-1}}}{b^{a_{i-1}} + b^{a_{i+1}}} \right) \frac{a_i^2}{1 + \kappa_T a_{i-1}^2} \\ \quad + T \left(\frac{p_{i+1} b^{a_i}}{b^{a_i} + b^{a_{i+2}}} \right) \frac{a_{i+1}^2}{1 + \kappa_T a_i^2} - T \left(\frac{p_i b^{a_{i+1}}}{b^{a_{i-1}} + b^{a_{i+1}}} \right) \frac{a_i^2}{1 + \kappa_T a_{i+1}^2} \\ \quad \text{with } i = 1, \dots, n \\ \\ a_{-1} = a_1 + 2\gamma \quad \text{and} \quad a_0 = a_1 + \gamma \\ a_{n+1} = a_n - \gamma \quad \text{and} \quad a_{n+2} = a_n - 2\gamma, \end{array} \right. \quad (6)$$

where the indices 0 and $n+1$ in the first equation express the coupling of p_i to a_i in the first ghost cells. This system can be written as the system of equations

$$F(\mathbf{U}, \boldsymbol{\lambda}) = \mathbf{0}, \quad (7)$$

where $F : \mathbb{R}^{2n+m} \rightarrow \mathbb{R}^{2n} : (\mathbf{U}, \boldsymbol{\lambda}) \mapsto F(\mathbf{U}, \boldsymbol{\lambda})$ with n the number of cells and m the number of parameters. \mathbf{U} is a $2n$ dimensional solution vector of the problem that contains both the p and a variables and $\boldsymbol{\lambda} \in \mathbb{R}^m$ denotes the set of parameters.

3 The trivial solution

In this section we search for a trivial solution of system (6), a solution we can calculate analytically that will be used as a starting point for the numerical continuation in section 5.

If we assume that the solution is homogeneous and homogeneous boundary conditions are applied, i.e $\gamma = 0$, then the values of p and a are the same for all cells so that

$$p_i = p_j \quad \text{and} \quad a_i = a_j \quad \forall i, j = -1, \dots, n+2. \quad (8)$$

The system (6) now reduces to

$$\begin{cases} 0 = \frac{\rho_{\text{PIN}_0} + \rho_{\text{PIN}} a_i}{1 + \kappa_{\text{PIN}} p_i} - \mu_{\text{PIN}} p_i & \text{for } i = 0, \dots, n+1 \\ 0 = \frac{\rho_{\text{IAA}}}{1 + \kappa_{\text{IAA}} a_i} - \mu_{\text{IAA}} a_i & \text{for } i = 1, \dots, n, \end{cases} \quad (9)$$

and

$$a_{-1} = a_0 = a_1 \quad \text{and} \quad a_{n+1} = a_{n+2} = a_n. \quad (10)$$

Because p_i and a_i are real positive numbers, the solution is given by

$$\begin{cases} p_i = \frac{-1 + \sqrt{1 + 4\kappa_{\text{PIN}} (\rho_{\text{PIN}_0} + \rho_{\text{PIN}} a_i) / \mu_{\text{PIN}}}}{2\kappa_{\text{PIN}}}, \\ a_i = \frac{-1 + \sqrt{1 + 4\kappa_{\text{IAA}} \rho_{\text{IAA}} / \mu_{\text{IAA}}}}{2\kappa_{\text{IAA}}}, \end{cases} \quad (11)$$

with $i = -1, \dots, n+2$. This is the trivial solution of the system.

From equation (9) we know that for a certain parameter set, there is only one trivial homogeneous solution. By formula (11) it is easy to calculate this trivial solution for different parameter values. Figure 5 shows the concentration of IAA in one cell (cell number 6) versus the parameter ρ_{IAA} . Because the solution is homogeneous, the trivial solution curve would be the same for every cell and is independent of the number of cells. Figure 5 denotes also the trivial solution for parameter set M1, M2 and M3 with a cross.

3.1 Stability of the trivial solution

We can calculate the trivial solution for every choice of the parameter, but, it will only be stable in a limited parameter range dependent on the number of cells. Although expression (11) for the trivial solution is simple, it is not easy to determine the stability of this solution. The Jacobian matrix of the coupled system (6) is not trivial and so are its eigenvalues. The stability can however be calculated by numerical means and in our simulations we approximate the Jacobian with central finite differences. The j -th column of $J(\mathbf{U}, \boldsymbol{\lambda})$ is $J(\mathbf{U}, \boldsymbol{\lambda}) \mathbf{e}_j$ where \mathbf{e}_j is the unit vector with the j -th component 1 and the other components 0. The column is then approximated as

$$J(\mathbf{U}, \boldsymbol{\lambda}) \mathbf{e}_j = \frac{F(\mathbf{U} + \epsilon \mathbf{e}_j, \boldsymbol{\lambda}) - F(\mathbf{U} - \epsilon \mathbf{e}_j, \boldsymbol{\lambda})}{2\epsilon}, \quad (12)$$

where ϵ is taken of the order of 10^{-7} .

The stability of the trivial solution for a row of 20 cells is shown in figure 5. For smaller values of ρ_{IAA} the eigenvalues of the trivial solutions lie in the left half-plane of the complex plane. Therefore these solutions are stable which is denoted with a full line in figure 5. For larger values of ρ_{IAA} , at least one eigenvalue lies in the right half plane and so the trivial solution is unstable. This is indicated with a dotted line.

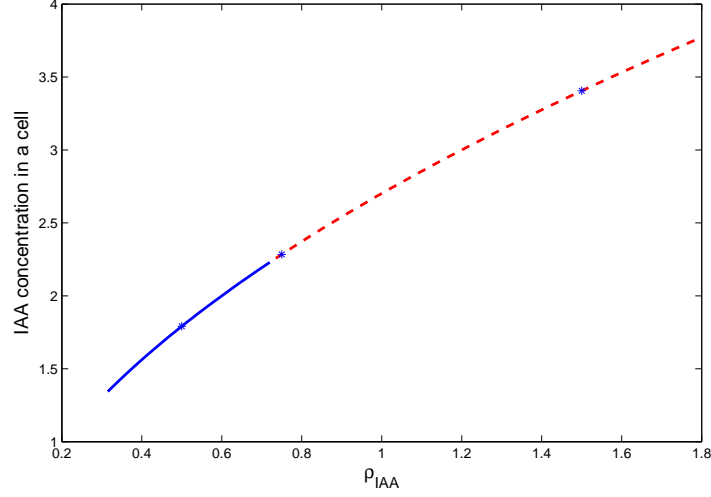


Figure 5: The concentration of IAA in the trivial solution as a function of the IAA production coefficient ρ_{IAA} . Each cell has the same concentration. However, for large ρ_{IAA} this solution becomes unstable. Stability is calculated for a row of 20 cells. The other parameters are taken from table 1.

Also for other parameter values we can calculate the stability of the trivial solution. In each plot on figure 6 two parameter values are varied. The other parameter values are taken as in parameter set M2. On these plots we see for which values the trivial solution is stable (marked in gray) and unstable (not marked) for a row of 20 cells. For example figure 6a shows that for very small values of ρ_{IAA} almost every value of T gives a stable trivial solution. All other values of ρ_{IAA} give an unstable trivial solution if T is not too small.

If we increase the number of cells, the shape of the stable region of the trivial solution remains approximately the same — it only gets slightly smaller.

4 Methods

4.1 Bifurcation analysis

The study of the relation between the stability of a solution and the parameters of the corresponding dynamical system is known as bifurcation analysis (Seydel, 1994). Such an analysis identifies the stable and unstable solutions and the bifurcation points that mark the transitions between them. This is biologically relevant since it will allow us to predict the patterns that emerge in the time evolution as the parameters of the model are changed. A bifurcation point is a solution $(\mathbf{U}_i, \lambda_i)$ of system (7) where the number of solutions changes when λ passes λ_i . There are several types of bifurcation points, for example the

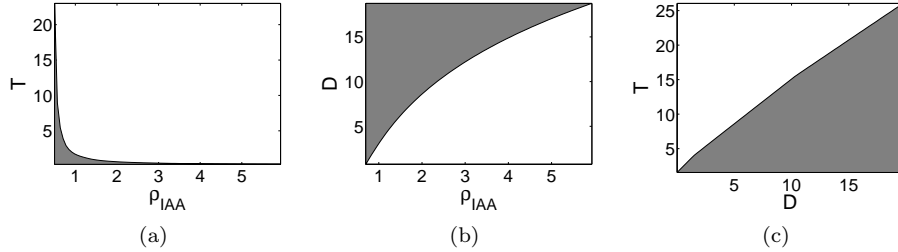


Figure 6: Stable (marked in gray) and unstable region of the trivial solution for a row of 20 cells and different choices of the parameters ρ_{IIA} (IAA production coefficient), D (IAA diffusion coefficient) and T (IAA transport coefficient). Other parameters are taken from parameter set M2.

branch points, limit points and Hopf bifurcation points. A Hopf bifurcation is a transition where a periodic orbit appears and branch points and limit points are both bifurcation points among steady state solutions. A limit point, also called a turning point, is a point where, locally, no solutions exist on one side of the limit point and two solutions on the other side. A branch point on the other hand is a point where two or more branches with distinct tangents intersect. This analysis usually leads to a bifurcation diagram that highlights the connections between stable and unstable branches as the parameters change. It is useful to track all these solution branches that emerge, split or end in a bifurcation point. This can be done with the help of numerical continuation methods.

4.2 Continuation methods

The system of equations (7) is a smooth map and we know that $\mathbf{0} \in \text{Range}(F)$. Following the implicit function theorem we know that for a regular point $\mathbf{x}_0 = (\mathbf{U}_0, \boldsymbol{\lambda}_0) \in \mathbb{R}^{2n+m}$ of F that satisfies $F(\mathbf{x}_0) = \mathbf{0}$, the solution set $F^{-1}(\mathbf{0})$ can be locally parameterized about \mathbf{x}_0 with respect to some parameter s . This means that the system of equations $F(\mathbf{U}, \boldsymbol{\lambda}(s)) = \mathbf{0}$ defines an implicit curve $\mathbf{U}(\boldsymbol{\lambda}(s))$ where $\boldsymbol{\lambda}(s) : \mathbb{R} \rightarrow \mathbb{R}^m$ is any parametric curve in the \mathbb{R}^m (Allgower and Georg, 1994). The idea of continuation methods is to find a curve c of approximate solutions \mathbf{U} of the system in function of the parameter $\boldsymbol{\lambda}(s)$. To construct such a curve of subsequent solution points $\mathbf{x}_i = (\mathbf{U}_i, \boldsymbol{\lambda}_i) = (\mathbf{U}_i, \boldsymbol{\lambda}(s_i))$, continuation methods use a starting point $\mathbf{x}_0 = (\mathbf{U}_0, \boldsymbol{\lambda}_0)$, a solution of system (7), along with an initial continuation direction (Krauskopf et al, 2007). This starting point is typically a trivial solution. An important family of the continuation methods are the predictor-corrector methods such as pseudo-arclength continuation. The idea of the algorithm is to first predict a new solution point. In the corrector step, this predicted point is the start value for an iterative method that will approximate the solution to a given tolerance. For the pseudo-arclength, the predictor step uses the tangent vector to the curve at a solution point and a

given step size to predict a guess for the next solution point on the curve. The corrector step improves the guess with Newton iterations.

Numerical continuation is available in AUTO (Doedel et al, 1997), LOCA part of Trilinos (Salinger et al, 2005), PyDS (Clewley et al, 2007) and others. These libraries can often also identify the bifurcations that occur along the continued curve and some of them, such as AUTO can automatically switch between branches at bifurcation points.

5 Results

In the next three examples we give, for a file of 20 cells, the numerical bifurcation analysis of problem (6) with respectively parameter sets M1, M2 and M3. In the last example we also give the results of the bifurcation analysis of problem (6) but now for a file of 100 cells instead of 20 cells and with parameter set M1.

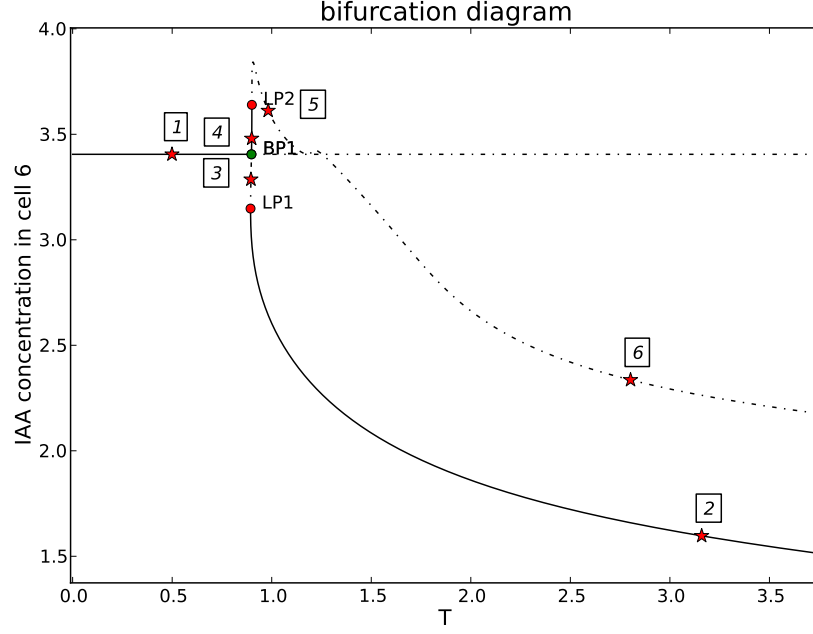
In each example we impose homogeneous Neumann boundary conditions and the IAA transport coefficient T is the continuation parameter. Each time we display the bifurcation diagram that denotes the IAA transport coefficient T versus the IAA concentration in cell number 6. Remark that we can construct the bifurcation diagram with any measure on the y-axis. We have chosen T as the continuation parameter similar to the one-dimensional simulations of Smith *et al.*. Also Jönsson *et al.* investigated the influence of the IAA transport coefficient T in their simplistic model by changing the ratio D/TP , with P the fixed value for PIN1.

We will find that the trivial solution loses its stability through either a branch point or a Hopf bifurcation.

Example 1. The results of the bifurcation analysis for parameter set M1 are shown in figure 7. Figure 7a shows the bifurcation diagram that depicts the concentration of the growth hormone auxin in cell number 6 versus the parameter T . The other plots in figure 7 show the steady state auxin patterns in all cells for the specific places indicated with labels in the bifurcation diagram. The trivial solution curve is the starting point of the continuation. It is the flat horizontal line in the bifurcation diagram. When the parameter T becomes larger than a critical value ($T = 0.8983$), the trivial solution loses its stability at a branch point. It was found by calculating for every solution $(\mathbf{U}_i, \boldsymbol{\lambda}_i)$ on the branch, the eigenvalues of the augmented Jacobian matrix defined as

$$J_{\text{aug}} = [J_{\mathbf{U}} | J_{\boldsymbol{\lambda}}]. \quad (13)$$

If the Jacobian $J_{\mathbf{U}}$ is singular and the rank of the augmented Jacobian is still smaller than $2n$, then the solution point $(\mathbf{U}_i, \boldsymbol{\lambda}_i)$ is a branch point. This means that there exist an eigenvalue $\mu(\boldsymbol{\lambda}_i)$ of the Jacobian which is equal to zero. Inserted into a graph, there is a path of an eigenvalue of the solution points corresponding to $\boldsymbol{\lambda}$ close to $\boldsymbol{\lambda}_i$, that crosses the imaginary axis at the real axis when $\boldsymbol{\lambda} = \boldsymbol{\lambda}_i$. In the branch point on figure 7 there is an exchange of stability



(a) Bifurcation Diagram

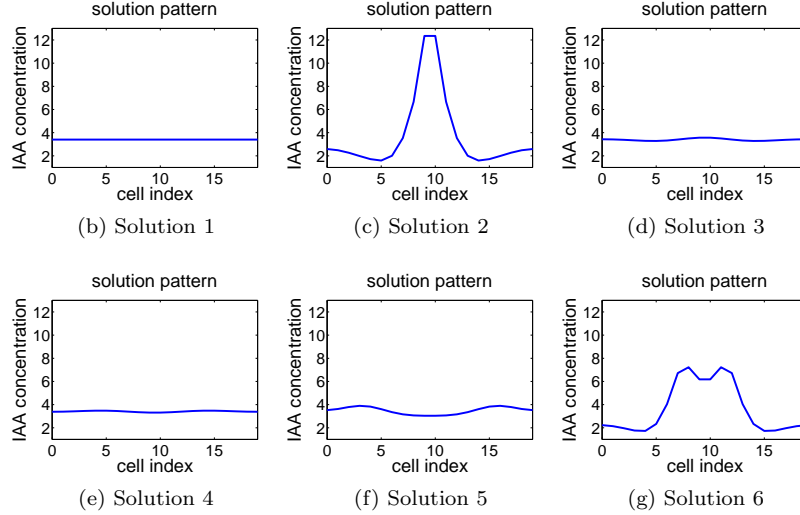


Figure 7: (a) The bifurcation diagram of example 1 for a row of 20 cells with continuation parameter T (IAA transport coefficient) versus the IAA concentration in cell number 6. Other parameters are taken from M1. BP denotes a branch point and LP a limit point. The stars mark the places of the figures displayed below.

(b)-(g) On these figures the IAA concentration in the whole domain is displayed corresponding with the stars marked on (a).

to another branch, also shown in the diagram. There are two stable parts on this other solution branch with patterns. When the IAA transport coefficient T is large, the stable solution pattern on this branch consist of one big peak (figure 7c). The other stable part on this branch appears in a very limited range where T is smaller. For example solution 4 is such a stable pattern and it has two small variations (figure 7e). The pattern in figure 7c is the same pattern that was obtained by numerical integration with the fourth order Runge Kutta in figure 4 as discussed in Section 2.2. We thus found a connection between the trivial flat solution and the numerical solution with peaks.

Example 2. The second example describes the results of the bifurcation analysis for the model with parameter set M2 that Smith *et al.* used in their publication (Smith et al, 2006). The difference with the first parameter set M1 is a lower production coefficient of IAA, ρ_{IAA} . In the previous example, the stability of the trivial solution was lost in a branch point where branches with steady state solutions intersect. Now, we find that the stability is lost through a Hopf bifurcation where the equilibrium transitions into a periodic orbit. Looking at the eigenvalues of the Jacobian in this Hopf point, there is a pair of eigenvalues that satisfies

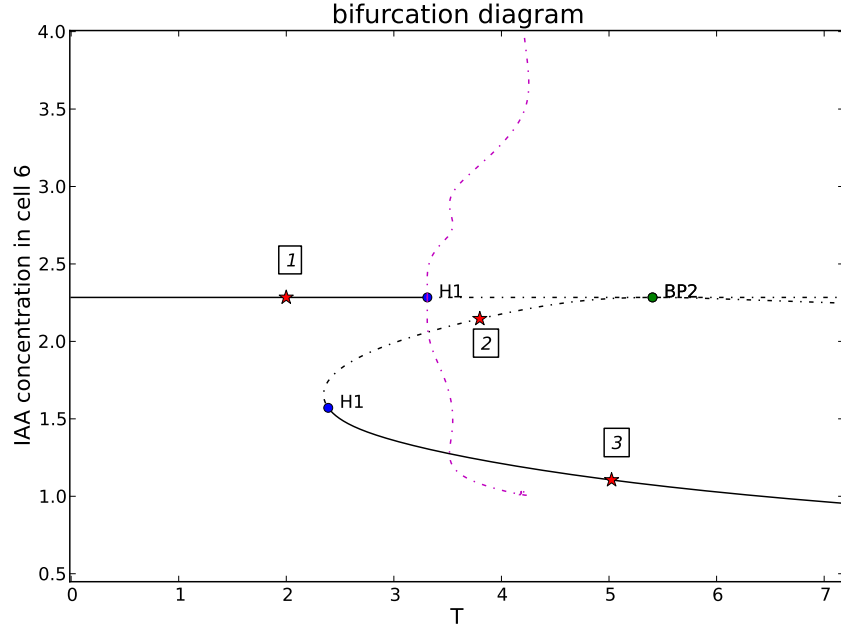
$$\mu(\lambda_i) = \pm i\beta. \quad (14)$$

If we draw a trajectory of the eigenvalues of solution points with λ close to λ_i , we see that there are two complex conjugated eigenvalues different from zero that cross the imaginary axis when $\lambda = \lambda_i$.

Figure 8a shows the bifurcation diagram depicting again the concentration of IAA in cell 6 versus the continuation parameter T but now for parameter set M2. In this situation, the stability of the trivial solution is lost in a Hopf point at $T = 3.3113$. The branch that emerges from this Hopf point, shows the maximal and minimal IAA concentration over the orbit for each choice of parameter T . All the solutions on this branch are unstable and therefore we only have unstable periodic solutions. Further, also another steady state branch, different from the trivial solution branch, is displayed. This branch intersects with the trivial solution branch at a branch point ($T = 5.4047$). Around this branch point, all solutions are unstable. However, when we follow this new branch, we encounter another Hopf point where we now gain stability. The pattern of these stable solutions consist of one single big peak in the middle of the domain (see figure 8d)

Example 3. For the third example parameter set M3 is used, which differs from sets M1 and M2 in the production coefficient of IAA. It is smaller than in set M2.

The resulting bifurcation diagram is shown in figure 9. Just like in example 2, the stability of the trivial solution is lost in a Hopf point ($T = 22.7384$). However, in contrast with this previous example, the periodic solution branch that intersects with the trivial solution branch in this point contains stable periodic solutions. Figure 10 shows, in a three dimensional plot, the stable



(a) Bifurcation Diagram

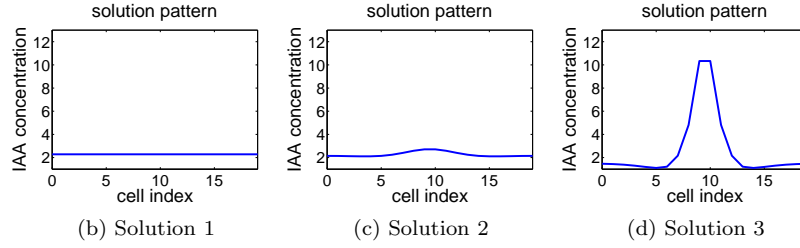


Figure 8: (a) The bifurcation diagram of example 2 for a row of 20 cells with continuation parameter T (IAA transport coefficient) versus the IAA concentration in cell number 6. Other parameters are taken from M2. The stars mark the places of the figures displayed below. The dotted line through point H1 shows the maximal and minimal value of the IAA concentration in cell number 6 of the periodic solution for each choice of the parameter T . H and BP denote respectively a Hopf point and a branch point. (b)-(d) On these figures the IAA concentration in the whole domain is displayed corresponding with the stars marked on (a).

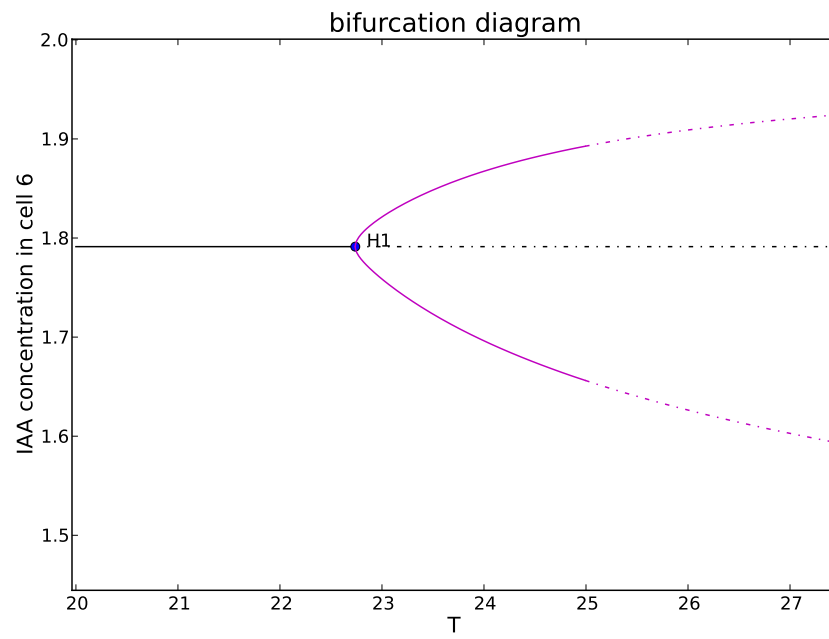


Figure 9: Bifurcation diagram of example 3 with parameter set M3. It depicts the continuation parameter T (IAA transport coefficient) versus the IAA concentration in cell number 6. H denotes a Hopf point. The stable orbit for $T = 23.5$ is shown on figure 10.

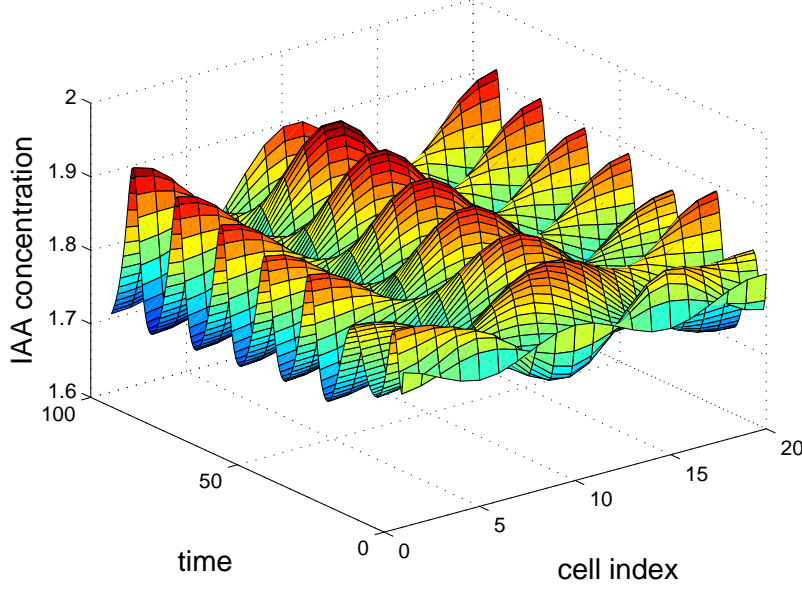


Figure 10: The time evolution for a row of 20 cells starting from the initial value in equation (15) with homogeneous Neumann boundary conditions, parameter set M3 but with IAA transport coefficient $T = 23.5$. We used RK4 for numerical integration. The resulting solution is a periodic solution where the pattern changes from one peak concentration of auxin in the middle of the domain to a pattern with high concentrations at the boundaries. The periodic solution corresponds with the solution for $T = 23.5$ on the periodic solution branch in figure 9.

periodic solution for IAA transport coefficient $T = 23.5$ found with RK4 starting from the initial value

$$p_i(0) = 1.79 \quad \text{and} \quad a_i(0) = 3.76, \quad (15)$$

where a small perturbation $0.02 \sin((5(i+2)\pi)/24)$ for $i = 1, \dots, 20$ was added. We see that the periodic solution changes in time from a pattern with one peak concentration of auxin in the middle of the domain to a pattern with two high auxin concentrations at the sides of the domain. In figure 11 we plotted this trajectory in the $(a_6(t), da_6(t)/dt)$ -plane starting from the initial value in equation (15).

Example 4. The previous three examples showed a part of the bifurcation diagrams corresponding with parameter sets M1, M2 and M3, that differ in IAA production rate, for a one dimensional domain of 20 cells. In the next

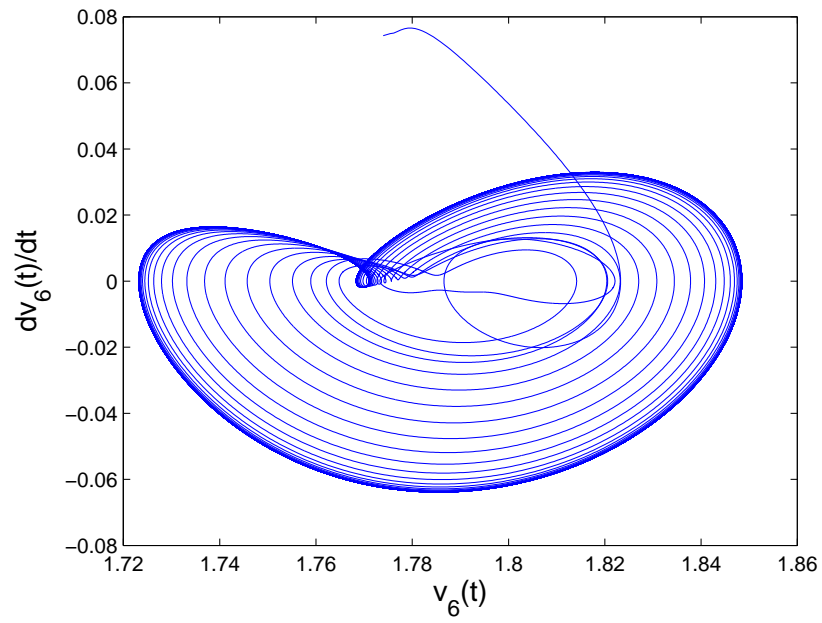


Figure 11: The trajectory of the time evolution of figure 10 in the $(a_6(t), da_6(t)/dt)$ -plane. We used a row of 20 cells starting from initial value (15) with homogeneous Neumann boundary conditions, parameter set M3 but with IAA transport coefficient $T=23.5$ and RK4 for numerical integration.

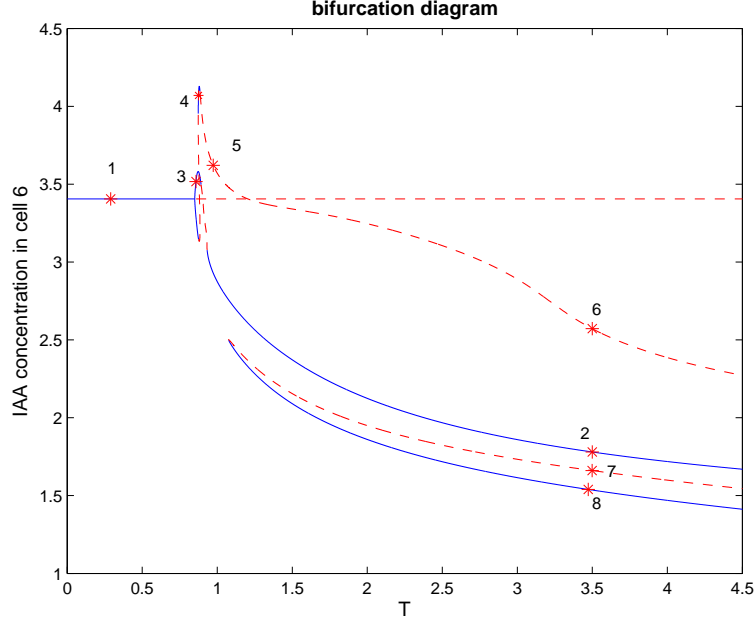
example we applied pseudo arc length continuation to a row of 100 cells and parameter values of set M1. In this example, the stability of the trivial solution is again, as in example 1, lost at a branch point ($T = 0.8504$) (see figure 12a). The branch that crosses the trivial solution branch in this point is a bit more complicated. The branch contains 3 different stable parts. The stable part that contains solution point 2 consists of solutions with a pattern with 8 peaks (see figure 12c). Also the small stable area on the branch that contains solution 3 consists of patterns with 8 peaks, but they are smaller due to the small value of T in this region. We see that the peaks become higher for an increasing IAA transport coefficient T (compare for example the patterns in figures 12c and 12d or in figures 12f and 12g). The third stable part on this solution branch, appears also in a limited range of T . The patterns show only 7 peaks of high auxin concentration (see figure 12e). The patterns on the unstable part of the branch that contains solutions 5 and 6 also consist of 7 peaks (see figure 12f and 12g)

The other solution branch in figure 12a is found by time integration by starting with the steady state solution of figure 4 or the pattern in figure 7c copied five times in a row which rapidly leads to a steady state that can be used as a starting point for the continuation. We see that this branch is not (directly) linked with the trivial solution branch and consists of one stable and one unstable part. On both parts the patterns consist of 9 high peaks of auxin concentration (see figures 12h and 12i).

Figures 7, 8, 9 and 12 for examples 1, 2, 3 and 4 show different bifurcation diagrams. In the examples 1 and 4, where parameter set M1 is used, the stability of the trivial solution is lost in a branch point. While in the examples 2 and 3 it is lost in a Hopf point. We can calculate the type of these bifurcation points for every transition from stable to unstable for the three dimensional space of the parameters D , T and ρ_{IAA} . We found that in the one-dimensional case, for a row of cells, only these two different situations can occur: either the stability of the trivial solution is lost in a Hopf point, or the stability is lost in a branch point. Figure 13 shows, for a row of 20 cells, parameter values from table 1, the parameters D , T and ρ_{IAA} , the corresponding type of bifurcation. For example figure 13a shows that for small values of the production coefficient of IAA the stability of the trivial solution will be lost in a Hopf point. Indeed, in example 2 and 3 we found similar results.

6 Conclusion and discussion

In this paper we have explored the model proposed by Smith et al (2006) for the transport of growth hormones in a one-dimensional row of cells. This model describes the evolution of the concentration of PIN1 and IAA in each of the cells by a coupled set of non-linear ordinary differential equations. The change in concentration of IAA in each cell depends only on PIN1 and IAA concentrations



(a) Bifurcation Diagram

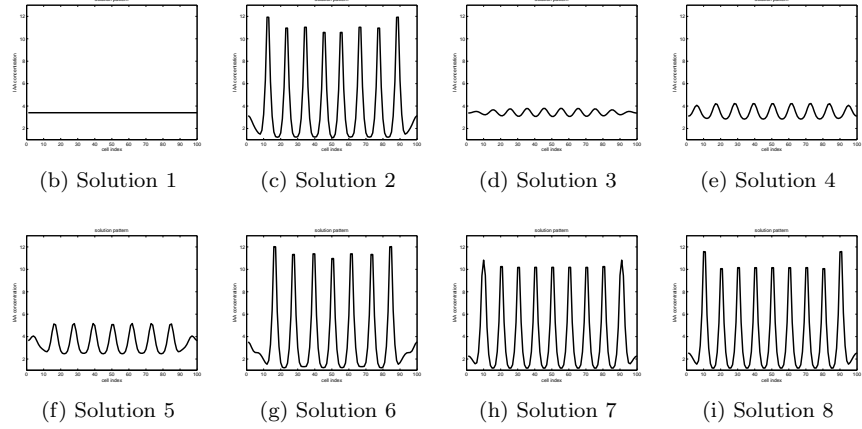
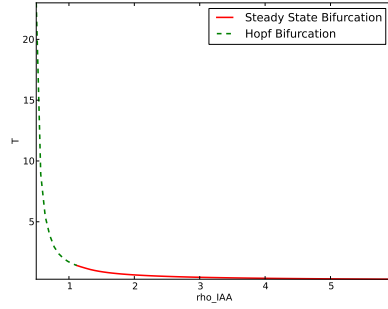
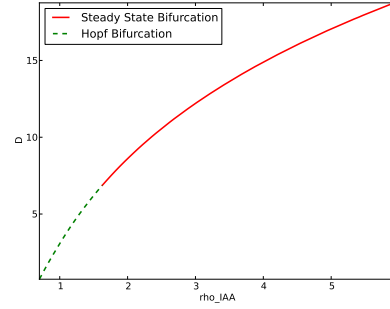


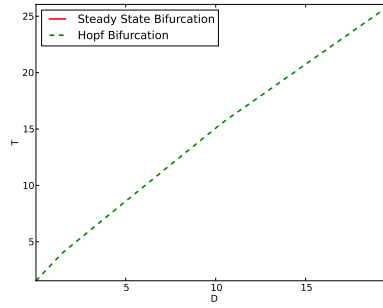
Figure 12: (a) Bifurcation diagram of example 4 for a row of 100 cells and parameter set M1. The diagram shows the continuation parameter T (IAA transport coefficient) versus the IAA concentration in cell number 6. The unconnected branch is found by time integrating the steady state solution of figure 7c copied five times in a row until a steady state is found. The resulting steady state is then used as a starting point for the continuation. The stars mark the places of the figures displayed below. (b)-(i) On these figures the IAA concentration in the whole domain is displayed corresponding with the stars marked on (a).



(a) $D = 1.000$



(b) $T = 3.500$



(c) $\rho_{IIA} = 0.750$

Figure 13: Map of types of bifurcation points for a row of 20 cells and different choices of the parameters ρ_{IIA} (IAA production coefficient), D (IAA diffusion coefficient), T (IAA transport coefficient). Other parameters are taken from table 1.

in that cell, its nearest and next-nearest neighbors and this leads to a sparsely coupled system.

We have analyzed the steady state solutions of the system as a function of three of the 11 parameters in the problem. We have varied the IAA transport coefficient T , the diffusion coefficient D and the production rate ρ_{IAA} . We have used numerical continuation to generate these solutions starting from a trivial solution of the system.

The trivial solution is identified as an analytical solution where the concentration in all the cells is the same. This solution is stable for some region of the parameter space. However, changing the parameters, for example, increasing the IAA transport coefficient T , destroys its stability. In contrast to the uncoupled system studied by Jönsson et al (2006), the eigenvalues of the Jacobian of this coupled system can not be easily analyzed analytically. The Jacobian now has a blocked sparse structure and its eigenvalues are studied numerically.

In the exploration of the solutions, we have identified two generic bifurcation scenarios through which the trivial solution loses its stability. These scenarios reappear for various choices of the parameters. In the first scenario, a stable solution can lose its stability through a branch point, where it becomes a pattern with regular spaced peaks of high auxin concentration. This solution was already found by Smith and collaborators by direct numerical simulation. The spacing and the height of the peaks in the pattern depends on the other parameters of the system.

However, we have found in the coupled system that the trivial state can also lose its stability through a Hopf bifurcation, where the Jacobian has two complex conjugate eigenvalues that become purely imaginary. For a limited parameter range this leads to stable periodic solutions, where the concentration in the cell changes periodically over time. However, for another range of parameters these periodic orbits are unstable and the trivial solution then loses its stability through an unstable orbit. The steady state solution then falls, beyond a parameter threshold, back to a pattern of regularly spaced peaks (see figure 8). These Hopf bifurcation and the periodic solutions are not present in the model studied by Jönsson where the PIN1 concentration is kept constant and all eigenvalues of the Jacobian are real.

These are the only two bifurcation scenarios that we have found at the stability boundary of the trivial solution for various choices of the 11 parameters in the model and for an increasing number of cells in the row.

Although the paper studies the steady state solutions of a rather academic model with a row of equal sized square cells, the authors believe it is a valuable contribution to our understanding of pattern formation by auxin accumulation since it builds the foundation for a rigorous bifurcation analysis of the steady state patterns in a two dimensional array of cells. We expect to find there a similar trivial solution that will lose again its stability as the parameters change and turn into regular patterns of high concentration peaks and time periodic solutions.

In this paper we have studied bifurcations with $\gamma = 0$, so called homogeneous Neumann boundary conditions. Similar studies can be done for inhomogeneous

Neumann boundary conditions, however, then there is no analytically solvable trivial solution. We have explored continuation in γ and found, amongst others, s-shaped bifurcation diagrams with double limit points. This leads to a hysteresis effect in the boundary conditions. This will be further explored in the future.

There are still many uncertainties in the current generation of models. Especially the large number of parameters and the uncertainty in their values is a reason for concern. By focusing on the qualitative properties of the transitions that appear in the models rather than on the states for particular choices of the parameters, we hope to understand more about the possible patterns that appear in real systems. It is valuable to calculate similar bifurcation diagrams for all the proposed models for auxin transport using the numerical continuation methods. This will allow the comparison of models across a range of parameters and check if they exhibit qualitatively the same transition if parameters change.

In real plants it is impossible to tune a parameter such as the transport coefficient T in a continuous way as is done in these calculations. It can only be changed in discrete steps in a plant by the introduction of, for example, mutations that compromise or enhance the auxin production or transport. Comparing such experiments with the model outcome will make it possible to refine the models to give a more realistic description of the biological system.

The bifurcation analysis also yields interesting new insights into the potential behaviors of the biological system. It is interesting to note that low values of the IAA transport coefficient lead to flat distributions of the auxin concentration, whereas high concentrations are required to establish sharp accumulation peaks. Indeed, experimental inhibition of auxin transport with NPA abolishes the normal narrow accumulation peaks and results in a much flatter auxin distribution pattern (Scarpella et al, 2006).

One especially interesting behavior is the oscillation obtained with a specific set of parameter values (Fig 11). This behavior has to our knowledge never been observed in the context of leaf development. However, in the root basal meristem, oscillating auxin concentrations have been observed and related to the regular induction of laterals along the growing axis of the root (De Smet et al, 2007).

One other characteristic unveiled by the bifurcation analysis is that across the region where a pattern of auxin accumulation peaks are generated, these peaks occur at very stable distances. This would imply that in the case of vascular patterning, the initial distance between veins is relatively stable, implying that observed differences in vascular density in mature leaves (Dhondt et al, 2011) largely result from differences in subsequent development. This is an example of a new hypothesis generated by modeling a biological process that can be experimentally validated and underlines the importance of systematic exploration of biologically relevant parameter variations.

It is important to repeat that we have kept the plant geometry fixed in the current model. It is an open question how the calculations can be extended to include cells to undergo growth and division.

Acknowledgments

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